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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,565	01/29/2004	Mary Mah Lee Ng	59419-010102	9294

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GREENBERG TRAURIG LLP
2450 COLORADO AVENUE, SUITE 400E
SANTA MONICA, CA 90404

EXAMINER	
SALVOZA, M FRANCO G	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 07/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/769,565	NG ET AL.	
	Examiner	Art Unit	
	M. Franco Salvoza	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-27, 44-70 is/are pending in the application.

4a) Of the above claim(s) 1-27, 48-51, 55-70 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *01/31/05, 02/07/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Invention I in the reply filed on April 20, 2006 is acknowledged. The traversal is on the ground(s) that: there must have been some semblance of unity upon the first restriction; to properly restrict, examiner must show that the inventions are independent or distinct and that a serious burden would be imposed; that additional classifications were noted for the alleged same subject matter (class 930, subclass 10) indicating new, arbitrary classifications; the invention is misunderstood, citing a lack of prior art documents to indicate more than one inventive concept; the different embodiments recited in the claims are of a similar nature.

This is not found persuasive because: As indicated in the previous restriction, further restriction was deemed necessary after reconsideration of the newly presented claims.

The application was filed under U.S. practice, and not as a 371 of a PCT application, eliminating any requirement for prior art to break unity or demonstrate lack of unity of invention in a Restriction Action.

As indicated in the previous Restriction, the method of Invention I is distinct from the method of Invention II for not only claiming different flaviviruses, but for further reciting patentably distinct structural components not claimed in Invention I (an antibody and competitive ligand).

Additionally, Inventions III (product claims 62-64; reciting an antibody and competitive ligand), Invention IV (product claims 62, 65; reciting a nucleic acid sequence); Invention VI (product claim 70, reciting a polypeptide) are distinct for being product claims reciting

structurally distinct components. One of ordinary skill in the art would recognize that a polypeptide, an antibody/competitive ligand, and a nucleic acid sequence are structurally distinct (a polypeptide can be an enzyme or constitute as few as two linked amino acids; antibodies commonly possess light chains and heavy chains; nucleic acids are polymers of nucleotides containing phosphate groups, sugar groups, and purine and pyrimidine bases, all of which are distinctly classified products).

Furthermore, Invention V (method claims 66-69; reciting a polypeptide) is further distinct for being method claims (distinguished from product claims) that uses a patentably distinct component (a polypeptide).

The requirement is still deemed proper and is therefore made FINAL.

Claims 52-54 are pending and under consideration.

Specification

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52, 53, 54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 52 recites a method for controlling entry of a flavivirus into a cell, the flavivirus exhibiting a flavivirus envelope protein, the flavivirus envelope protein comprising a domain III of the flavivirus envelope protein, the method comprising administering to the cell an agent functionally interfering with the domain III of the flavivirus envelope protein.

Claim 53 recites the method of claim 52 wherein the domain III has a sequence substantially homologous to SEQ ID NO: 20 or SEQ ID NO:21.

Claim 54 recites the method of claim 52 wherein the agent hybridized to the Domain III has a sequence substantially homologous to SEQ ID NO: 20 or SEQ ID NO:21.

It is unclear what applicant intends by the recitations "functionally interfering." The specification refers to "any kind of interference with the functionality of the molecule," but encompasses more than merely inhibiting, but it is not clear what constitutes interference.

It is also unclear what applicant intends by the recitations "substantially homologous." The specification lists at least about 50% to most preferably 95-98% but such a range is indefinite.

Claim 54 is also rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 54 recites the limitation "wherein the agent hybridized to the Domain III" in reference to claim 52. However, claim 52 does not recite "the agent hybridized to the Domain III." There is insufficient antecedent basis for this limitation in the claim. Further, no clarification is provided by the specification as to an interpretation of "wherein the agent hybridized," as the term is usually used in the context of nucleic acids, and SEQ ID NOs 20 and 21 recite proteins as indicated in Example 22. Further, it is not clear whether the agent or the domain III has a sequence substantially homologous to SEQ ID Nos 20 and 21.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 52 recites a method for controlling entry of a flavivirus into a cell, comprising administering to the cell an agent functionally interfering with the domain III of the flavivirus envelope protein. Claim 53 recites wherein the domain has a sequence substantially homologous to SEQ ID NO: 20 or SEQ ID NO: 21. Claim 54 recites the method wherein the agent hybridized to the Domain III has a sequence substantially homologous to SEQ ID NO: 20 or SEQ ID NO: 21.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.
>
> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. In this case, the specification has not provided sufficient examples or structural characteristics regarding an agent that functionally interferes with domain III of the flavivirus envelope protein to provide adequate support for the entire scope of the genus claimed. While disclosing antibodies, competitive ligands and nucleic acids, the specification lacks a description of what other agents would be deemed to functionally interfere with domain III as well as what portions of the nucleic acids and antibodies must be conserved to still retain and maintain adequate structural and functional characteristics to participate in the required binding.

While the specification discloses blocking antibodies, ligands such as fibronectin and RGD peptides, proteases, and short interfering RNAs, no further information beyond these products is provided by the disclosure as to what indicates functional interference and what

portions of nucleic acids, antibodies and peptides must be conserved to provide support for the entire scope of the claim. Thus, the claims are drawn to a genus of agents without a supporting disclosure of what constitutes functional interference, what other agents functionally interfere, and what portions of the disclosed agents must be conserved to maintain adequate characteristics to participate. When a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a recitation to an agent that functionally interferes with domain III of flavivirus envelope protein. There is not identification of any domains of peptides, active sites of enzymes, or nucleotide sequences that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written support of the claimed genus.

Claims 52, 53 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific portion of domain III, does not reasonably provide enablement for the entire domain III. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. 112 P 1, the courts have put forth a series of factors. See, In re Wands, 8 USPQ2d 1400, at 1404 (CAFC 1988) and Ex Parte Forman, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. Id. While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

In this case, the factors of the quantity of experimentation necessary; the amount of direction or guidance presented; the presence or absence of working examples, the state of the prior art, and the breadth of the claims are most relevant.

As indicated above, claims 52, 53 broadly recite a method for controlling entry of flavivirus into a cell comprising administering to the cell an agent functionally interfering with domain III; wherein the domain III is substantially homologous to SEQ ID NOs 20 and 21.

As indicated in applicant's disclosure, references reviewing the state of the art such as Beasley et al. teach a variety of epitopes and subportions of domain III, the interference of which would result in effective neutralization of the virus. Further Beasley et al. teaches that antibodies that recognize these epitopes differed between virus strains and mutation at other amino acids created antigenic variation (p 13097, 9).

Applicant also discloses that SEQ ID NOs 20 and 21 are 400-500 amino acids in length, and example 22 shows the production of antibodies to the about 40 amino acid recombinant

domain III from amino acids 350 to 390. However, the disclosure does not sufficiently teach epitopes beyond example 22 to enable the full scope of the claim reciting domain III.

In view of the breadth of the claims, the lack of examples or guidance, and the fact that those in the art would not be able to determine without extensive experimentation how to use agents that functionally interfere for the full scope of the claim to domain III, the application has not provided sufficient information to enable those in the art to practice the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 52 is rejected under 35 U.S.C. 102(b) as being anticipated by Crill et al. (2001).

Claim 52 recites a method for controlling entry of a flavivirus comprising a flavivirus envelope protein comprising a domain III into a cell, the method comprising administering to the cell an agent functionally interfering with the domain III of the flavivirus protein.

Crill et al. teaches a monoclonal antibody that binds to domain III of a flavivirus (here Dengue) which blocks or interferes with the virus adsorption to cells (p. 7769).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 53 is rejected under 35 U.S.C. 103(a) as being unpatentable over Crill et al. in view of Beasley et al. (2002).

Claim 53 recites the method of claim 52 wherein the domain III has a sequence substantially homologous to SEQ ID NO: 20 or SEQ ID NO: 21.

See the teachings of Crill et al. above.

Crill et al. does not teach wherein the domain III has a sequence substantially homologous to SEQ ID NO: 20 or SEQ ID NO: 21.

Beasley et al. teaches neutralizing epitopes within structural domain III of the flavivirus West Nile Virus envelope protein including one with 88.7% homology to SEQ ID NO: 20 (see Result 2, 20.rge) and one with 99.1% homology to SEQ ID NO: 21 (Result 2, 21.rup).

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the method of Crill et al. and the domain III sequences of Beasley et al. because Crill et al. teaches that domain III encodes the primary flavivirus receptor binding motif and Beasley et al. teaches neutralizing epitopes within Domain III of West Nile virus, also a flavivirus.

One of ordinary skill in the art at time the invention was made would have had a reasonable expectation of success for using combine the method of Crill et al. and the domain III sequences of Beasley et al. because both Crill et al. and Beasley et al. teach that domain III of

flavivirus contains epitopes for use with neutralizing monoclonal antibodies.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Crill et al. and Beasley et al. in view of Wu et al. (2001).

Based on the recitation to "agent hybridized" and the lack of clarifying information in the specification, it is unclear what applicant intends in claim 54 (See Claim Rejections, 112 2nd paragraph above). However, the following is one interpretation of the claim.

Claim 54 recites the method of claim 52 wherein the agent hybridized to the domain III has a sequence substantially homologous to SEQ ID NO: 20 or SEQ ID NO: 21.

See the teachings of Crill et al. and Beasley et al. above.

Crill et al. and Beasley et al. do not teach wherein the agent hybridized to the domain III has a sequence substantially homologous to SEQ ID NO: 20 or SEQ ID NO: 21.

Wu et al. teaches peptide ligands that mimic the conformational epitope on domain III of the Japanese encephalitis virus, a flavivirus.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the method and domain III sequences of Crill et al. and Beasley et al. and the peptide agents of Wu et al. because Wu et al. teaches that peptide ligands mapped to domain IIIs elicit specific neutralizing antibodies in mice.

One of ordinary skill in the art at time the invention was made would have had a

reasonable expectation of success for using the method and domain III sequences of Crill et al. and Beasley et al. and the peptide agents of Wu et al. because both Crill et al., Beasley et al. and Wu et al. all teach that domain III of flavivirus contains epitopes that elicit specific neutralizing monoclonal antibodies.

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

The sequence search results enclosed disclose many polypeptides having substantial homology to SEQ ID Nos 20 and 21.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to M. Franco Salvoza whose telephone number is (571) 272-8410. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

M. Franco Salvoza
Patent Examiner
June 30, 2006

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600